

Claims

1. A method for determining the function or effect of a genetic element or a chemical modulator from a library of said genetic elements and chemical
5 modulators of known and unknown function on a population of cells comprising
- i) determining the distribution of an indicator nucleic acid sequence
being expressed in said cells in the presence and the absence of a first
10 chemical modulator, which modulator affects said distribution of said
indicator, wherein the cells are both co-expressing an effector nucleic
acid sequence and are in the presence of a second chemical modulator;
and
- ii) analysing the distribution data from all combinations of said effector,
15 modulator and indicator to derive functional linkages and assign function
to the effector and said second modulator.
2. A method for determining the function or effect of a genetic element or a
chemical modulator from a library of said genetic elements and chemical
20 modulators of known and unknown function on a population of cells comprising
- i) determining the distribution of an indicator nucleic acid sequence
being expressed in said cells in the presence of a first chemical modulator,
which modulator affects said distribution of said indicator, wherein the cells
25 are both co-expressing an effector nucleic acid sequence and are in the
presence of a second chemical modulator;
- ii) comparing the distribution data of i) above with known distribution
data, stored on an electronic or optical database, for the indicator nucleic
30 acid sequence in the absence of said first chemical modulator; and

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iii) analysing the distribution data from all combinations of said effector, modulator and indicator to derive functional linkages and assign function to the effector and said second modulator.

5 3. The method according to either of claims 1 or 2, wherein the effector nucleic acid sequence encodes a protein or peptide and is selected from the group consisting of DNA, cDNA, RNA and Protein Nucleic Acid.

10 4. The method according to any of claims 1 to 3, wherein the effector nucleic acid is an antisense oligonucleotide.

5. The method according to any of claims 1 to 3, wherein the effector nucleic acid is a small interfering RNA (siRNA) which causes gene silencing.

15 6. The method according to any of claims 1 or 5, wherein the effector nucleic acid comprises a nucleic acid sequence in a cellular expression vector.

20 7. The method of claim 6, wherein said expression vector is selected from the group consisting of plasmid, retrovirus and adenovirus.

8. The method according to any of claims 1 to 7, wherein the indicator nucleic acid sequence comprises a detectable label or encodes a detectable label.

25 9. The method according to claim 8, wherein the indicator nucleic acid sequence is created by fusing the effector sequence to a nucleic acid sequence encoding a detectable label.

30 10. The method according to either of claims 8 or 9, wherein said detectable label is selected from the group consisting of fluorescent protein, enzyme, antigen and antibody.

11. The method according to claim 10, wherein said fluorescent protein is a modified Green Fluorescent Protein (GFP) having one or more mutations selected from the group consisting of Y66H, Y66W, Y66F, S65T, S65A, V68L,
5 Q69K, Q69M, S72A, T203I, E222G, V163A, I167T, S175G, F99S, M153T, V163A, F64L, Y145F, N149K, T203Y, T203Y, T203H, S202F and L236R.
12. The method according to claim 11, wherein said modified GFP has three mutations selected from the group consisting of F64L-V163A-E222G, F64L-
10 S175G-E222G, F64L-S65T-S175G and F64L-S65T-V163.
13. The method according to claim 10, wherein said enzyme is selected from the group consisting of β -galactosidase, nitroreductase, alkaline phosphatase and β -lactamase.
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14. The method according to any of claims 1 to 13, wherein the modulator is selected from the group consisting of organic compound, inorganic compound, peptide, polypeptide, protein, carbohydrate, lipid, nucleic acid, polynucleotide and protein nucleic acid.
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15. The method according to any of claims 1 to 14, wherein the modulator is selected from a combinatorial library comprising similar organic compounds such as analogues or derivatives.
- 25 16. The method according to any of claims 1 to 15, wherein said cell is an eukaryotic cell.
17. The method according to claim 16, wherein said eukaryotic cell is selected from the group consisting of mammal, plant, bird, fungus, fish and
30 nematode, which cell may or may not be genetically modified.

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18. The method according to claim 17, wherein said mammalian cell is a human cell, which cell may or may not be genetically modified.

5 19. The method according to any of claims 1 to 18, wherein the distribution of the indicator nucleic acid is determined using an imaging system.

20. An automated system for determining the function or effect of a chemical and /or a genetic element on a population of cells comprising use of the method according to any of claims 1 to 19 together with an imaging system and a
10 computerised data processing device.

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